

Aus der Medizinischen Universitäts-Poliklinik Basel

(Direktor: Prof. Dr. O. Gsell)

The Occurrence of Hyperparathyroidism in Various Members of Seven Families

Inaugural-Dissertation

zur Erlangung der Doktorwürde der Medizinischen Fakultät
der Universität Basel

vorgelegt von

S. Leonard Phillips

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I. Introduction.

The occurrence of familial cases of hyperparathyroidism is of essential importance. It supports the assumption of hereditary influences in the appearance of adenomas of the parathyroid glands. In 1936 the first familial observation of hyperparathyroidism referring to two siblings was published, 72 years after the first description of multiple cystic formations in the human skeleton coupled with increased calcium excretion in the urine by Engel 1864, and 40 years after the presentation of the classical paper of Recklinghausen concerning "General hyperparathyroidism of the skeleton with cystic formations". 1904 Askanazy suspected the relationship between parathyroidal gland and decalcification of the skeleton in a case of ostitis fibrosa. 1926 Mandl removed for the first time an adenoma of the parathyroidal glands in a patient suffering from ostitis fibrosa generalisata with prompt normalisation of the calcium metabolism. The sister of this patient had ostitis fibrosa localisata of the tibia which gave rise to spontaneous fracture and later developpment into a sarcoma. Since 1936 several observations of ostitis fibrosa generalisata in various members of a family have been reported, but this has been a rare event. In combination with the report of a new family with 3 cases of ostitis fibrosa generalisata and 3 cases of nephrolithiasis we have collected the scattered publications on this subject and present the problem in detail.

II. Published cases.

Of the 600-750 estimated cases of hyperparathyroidism reported since 1925, there appears a distinct *familiar tendency* to the disease in *only six families* or in fifteen individuals, not including our cases.

A. First *Goldman* and *Smyth* in 1936 reported the occurrence of hyperparathyroidism in two siblings (case I and II).

CASE I (*Goldman* and *Smyth*). An Italian girl, 17 years old, of short stature, was admitted to hospital in California with a waddling gait, left pathological fracture of the neck of the humerus, diagnosed as a giant cell tumor. Polydipsia, polyuria, constipation, increased fatigability, severe attacks of left ureteric colic, and pain in left humerus and right tibia were reported. A visible tumor was found in the left thyroid gland area. Laboratory reports of a remarkable character: Serum calcium 19.2 mg.%, plasma alkaline phosphatase 33.2. Kay-Jenner units per 100 c.c. of blood. The calcium balance was markedly negative. The urine was cloudy: there were 20-25 red blood cells per high dry microscopic field. Intramuscular phenolsulphthalein excretion was 55% in two hours. The electrocardiogram showed a shortened Q-T and other changes indicative of cardiac muscular hypotonicity. Roentgenograms revealed generalized demineralization, cysts in humeri, right tibia, metacarpals and pubic bones. Several small calculi in the left kidney. Barium retention in the stomach after six hours. A parathyroid adenoma, weighing 11.8 grams, and measuring 3.7 cm. by 2.8 cm. by 3 cm. was removed from within the capsule of the left lobe of the thyroid at its inferior pole. Histopathology: water-clear cells predominated, also smaller groups of chief cells and transitional wasserhelle forms and some light oxyphil cells. Recovery uneventful except for tetany on third post operative day (serum calcium 8.8 mg.%).

CASE II (*Goldman* and *Smyth*). Her brother, 23 years old, was then being treated for giant cell tumor of the mandible. There was a painful swelling at the mandibular symphysis. Later a spontaneous fracture occurred here. Biopsy showed a giant cell tumor. Roentgen therapy provided no improvement. He developed general malaise and fatigability. He was a well developed man, also of short stature. A small nodule was palpable in the lower left thyroid region. Serum calcium 17.5 mg.%, plasma alkaline phosphatase 10.3 Kay-Jenner units per 100 c.c. of blood, serum phosphorus 1.5 mg.%. Marked negative calcium balance. Urine normal except for 10 pus cells per high dry microscopic field. Blood sugar estimate 68 mg.%. Blood Wassermann and Kahn showed four plus reaction. Basic metabolic rate was minus 23. Q-T shortened. Roentgenograms revealed generalized skeletal demineralization. Mandibular cyst and a small cyst in one phalanx. No renal calculi. Esophageal roentgenogram showed dextral notched deviation below laryngeal level. An adenoma of the left inferior parathyroid weighing 6.5 grams, measuring 3 by 2 by 2 cm was found. The palpable nodule proved to be small thyroid adenoma. The parathyroid adenoma was composed of chief cells, no water clear cells seen. No tetany appeared. Recovery was uneventful.

No signs of HP were found in other members of the family. Both siblings were in the same age group when the symptoms occurred. The location of the tumor in both was identical, the histology varied. Both had skeletal symptoms; one renal involvement. As *Albright* points out, where considerable alkaline phosphatase is present and rapid calcium deposition in the bones

occurs after parathyroidectomy, tetany can be expected. The question arises if the brother with 68 mg.% sugar did not have latent pancreas islet involvement.

B. *Schneider, Kyger, and McCullagh* report two familiar cases (original literature not available however).

CASE III (*Schneider et al.*). 20-year-old pregnant woman. Adenoma weighing 8.5 grams, consisting largely of dark oxyphilic cells.

CASE IV (*Schneider et al.*). Her second cousin once had polycystic bone disease and a parathyroid adenoma. Section of cousin's tumor revealed tumor largely of dark oxyphile variety.

Rather than a contraindication to parathyroidectomy, removal of the adenoma sustained the gestation.

C. Two Norwegian sisters with primary HP came to the attention of *Nielsen*:

CASE V (*Nielsen*). Female, age 47, had been ill during past ten years with pyelitis and renal calculi. Six years prior to admission she experienced fatigue, indisposition, and rheumatoid pain in both legs and lumbar region. She could not walk without aid of crutches. She complained of nausea, anorexia, loss of weight, and constipation. Her family noticed a pronounced change of character; the patient was unbalanced, depressed, and had had delusions. On physical examination scattered skin suggillations, chipped fingers, and plum-sized tumor palpable below sternal end of left sternocleidomastoid muscle were found. Serum calcium 14 mg.%, serum phosphorus 5.7 mg.%, serum alkaline phosphatase 21 Bodansky units. Radiological examination revealed halisteresis and small cysts in tibia and fibula. A walnut-sized tumor, 4 by 2½ by 2½ cm., was removed from left lower thyroid pole. The author described the histology as "typical". Postoperative course was uneventful and promising.

CASE VI (*Nielsen*): Female, aged 33, sister of V, had long history of fatigue, indiposition, rheumatic pain, and gait impairment. Serum calcium 14.0 mg.%, serum phosphorus 2.4 mg.%, increased calcium excretion in the urine. Roentgenograms showed pronounced calcium and numerous scattered cysts. No parathyroid tumor was found at operation. Patient discharged from hospital unable to walk. Her disablement increased. Seven years later she died of uremia. There is no record of a necropsy.

The operation on patient VI was performed in 1932, when knowledge concerning aberrant parathyroid tumors (in up to 25% of the cases of parathyroid adenomas (*Mandl*) was meager.

D. The unique occurrence of parathyroid adenoma in father and daughter was reported by *Shallow and Fry*.

CASE VII (*Shallow and Fry*). The father, a physician, 35 years old, was subject to spontaneous fracture of surgical neck of right humerus and comminuted fracture of both femurs. Laboratory studies revealed anemia and trace of albuminuria. Radiological examination revealed bone changes typical of Morbus Recklinghausen or multiple myeloma. At 26 years a duodenal ulcer diagnosis was substantiated by roentgenogram. Gastrointestinal distress had occurred continually since. Polyuria and polydipsia present. Patient was nervous and irritable. His gait showed a marked shuffling tendency. He complained of boring pain in all extremities at night. A mass was palpated on the lower left lobe of the thyroid. Serum calcium was 13 mg.%.
Operation yielded a tumor in the capsule of the lower left thyroid measuring 3.3 by 3.2 by 3.1 cm.; wasserhelle cells predominated. No tetany occurred postoperatively. Patient improved considerably.

Fifteen years after the first parathyroid operation, the patient was readmitted with almost identical symptoms, except no spontaneous fractures. His urine was normal except for the fixed specific gravity of 1,007-1,009. Urea clearance was 40% of normal. Serum calcium 15.8 mg.%, serum phosphorus 2.1 mg.%, alkaline phosphatase 6.3 Bodansky units. Roentgenograms showed halisteresis and cystic areas in scapsula, ulna, femur, tibia, and ribs, and bilateral nephrocalcinosis.

Operative removal of a nodule measuring 4.2 by 2.6 by 2.3 cm. to the right of the esophagus and behind the recurrent nerve was performed. The patient developed on the fourth post-operative day tetany. Eleven days after operation he despite continual calcium lactate and vitamin D therapy had a serum calcium of 7 mg.% and serum phosphorus of 3.6 mg.%. He was discharged.

Three months later, readmission in stupor. Anamnesis of emesis reported. Urea 40 mg.%, creatinin 2.4 mg.%. 30% of Bromosulphalein was excreted in 30 minutes. Serum amylase 400 units. Serum calcium 6 mg.%, Serum phosphorus 6.5 mg.%. Alkaline phosphatase 9.9 Bodansky units. Seven weeks later—of what appeared to be a cerebral hemorrhage, he succumbed. No autopsy performed.

The assumption of two adenomas at the initial operation is questionable. The size of the first adenoma $3.3 \times 3.2 \times 3.1$ cm. corresponds to the first serum calcium value of 13 mg %, if one chooses to follow *Castleman's* and *Mallory's* rough scheme of correlation between size of adenoma and calcemia. Prolonged existence of a parathyroid tumor is usually prerequisite for nephrocalcinosis. The absence of tetany lends credence to the assumption of dual adenomas at the first operation. The hyperparathyroidism through arterial calcification probably was responsible for the direct cause of death.

CASE VIII (*Shallow and Fry*). His daughter, thirteen years old, was admitted with a shuffling gait, similar to that of her father. She had complained of loss of stamina during the last half year. Serum calcium 15.4 mg.%, serum phosphorus 1.8 mg.%, alkaline phosphatase 62 Bodansky units.

One year prior to admittance she had sustained a fracture of the surgical neck of the left humerus following a severe fall, which was probably not a pathological fracture. Roentgenogram at that time showed no underlying bone discrepancy. On the left lower thyroid pole a small regular mass was palpable (on present admission). Radiological studies showed demineralization of long bones and calvaria, fuzziness and increased density of metaphyseal region. One adenoma attached to left lower thyroid pole was removed. The tumor measuring 2.7 by 2.5 by 2.2, was mainly of the chief cell type with a few small groupings of oxyphilic forms. No postoperative complications. Seven years later re-examination showed normal blood and skeletal findings.

The mother and other siblings were scrutinized and found normal. The similarity in location of tumor is interesting. The clinical symptoms developed at different ages, and not at the same time. The pathology in both cases shows no parallel. No study of diet, water supply, etc. was made.

E. Five siblings, each showing symptoms of hyperparathyroidism, confirmed operatively by presence of one or more parathyroid adenomas, are described by *Frohner* and *Wolgamot*. The father died at 63, having suffered for fifteen years from polyuria, nycturia, weakness, kyphosis, and of renal failure—symptoms typical of hyperparathyroidism. No necropsy reports were available. The mother and two other siblings, having been screened, were found in good health.

CASE IX (*Frohner and Wolgamot*). A 25-year-old married female, of short stature, complained of pain in right hip in August 1947. Left frontal skull prominence appeared after birth of first child. Tachycardia, lassitude, generalized aches and pains—all were accentuated after birth of second child. She had lost thirty-five pounds. A firm nodule was palpable on inferior pole of right thyroid. There was also dorsal kyphosis and marked clubbing of the fingers. BMR + 18. Roentgenograms showed generalized skeletal demineralization, multiple bone cysts, fracture of left femoral neck and bilateral nephrocalcinosis. Sella turcica appeared normal. Serum calcium 15.98 mg.%, serum phosphorus 2.2 mg.%, alkaline phosphatase 15.96 Bodansky units. There was a trace of albuminuria. From right lower pole of thyroid a 3 by 2 by 1.3 cm. adenoma was removed. Mild tetany appeared on second postoperative day.

Five years after adenoma extirpation patient experienced renal colic. Her blood pressure had risen from 125/70 to 170/120. 17.5% intramuscular PSP dye excreted in thirty minutes. Serum calcium 9.6 mg.%, serum phosphorus 2.4 mg.%, alkaline phosphatase 2.1 Bodansky units. No further information obtainable.

CASE X (*Frohner and Wolgamot*). Her younger sister had suffered for two years with polyuria, nycturia and mild backache. She had lost two inches

in height in the past six years. A fracture at age 10 had healed rapidly. In February 1952, then 25, she broke her arm. Marked dorsal kyphosis and depression of lower sternum noted. Roentgenological studies showed general demineralisation with many cystic areas, and fracture through cyst in humerus. Lamina dura was absent. Serum calcium 14.4-19.5 mg.%, serum phosphorus 2.3 mg.%, alkaline phosphatase 6 Bodansky units per 100 c.c. blood. A right lower pole parathyroid adenoma 3.5 by 2 by 2 cm, weighing 12 grams, was extirpated. Tetany was manifest on the second day after the operation.

Seven months after operation with calcium 12.5 mg.%, serum phosphorus 2.2 mg.%, a second operation was performed since demineralisation and general malaise persisted. An adenoma, 1.5 by 1.0 by 1.0 cm., was found in left superior thyroid lobe and removed. Tetany appeared on second post-operative day. Thereafter steady improvement.

Tetany manifestation was no certain criteria for complete removal of overfunctioning parathyroid tissue.

CASE XI (*Frohner and Wolganot*). The brother, 29 years old, was diagnosed as a primary hyperparathyroidism on survey. His only complaint was mild chronic constipation. Twelve years previous he had experienced severe attacks of renal colic and hematuria. A stone was then removed. Patient drinks one glass of milk daily. Bilateral shotty node were palpated in the neck region; no skeletal changes were seen on roentgenological examination; a staghorn calculus was found in the left kidney. Serum calcium 13.3-13.6 mg.%, serum phosphorus 1.3-2.2 mg.%, alkaline phosphatase 1.2 Bodansky units per 100 c.c. Blood. Urinalysis: albuminuria + 1, specific gravity 1.015, 100 white blood cells per high dry microscopic field, and several grams negative rods. Left kidney was removed. A week later, two parathyroid adenomas from the left inferior pole of the thyroid (1.9 by 1.3 by 1.5 cm., 1.5 grams) and from the right inferior pole (1.3 by 0.9 by 0.8 cm., 0.6 grams) were removed. Recovery uneventful.

CASE XII (*Frohner and Wolgamot*). Aged 30, married and mother of two children, was diagnosed on survey, May 1952. She drinks one glass milk daily. In the neck a one cm. nodule was palpable on left upper thyroid pole plus numerous small bilateral cervical nodes. Serum calcium 16.8-18.1 mg.%, serum phosphorus 2.0-2.1 mg.%, alkaline phosphatase 4.8 Bodansky units. Blood sedimentation rate 22 mm./hr. Roentgenograms revealed minimal demineralization of skull and mandible. Lamina dura was absent. Bilateral nephrocalcinosis. From left superior thyroid pole an adenoma weighing six grams and measuring 2.5 by 2 by 1.7 cm., composed of dark oxyphilic cells, and from the right superior pole an adenoma, of the same histological character and measuring 1.5 by 1 by 1 cm. and weighing 2.5 grams were removed. Tetany developed on second post-operative day. Recovery was uneventful.

CASE XIII (*Frohner and Walgamot*). Again on survey, this 26-year-old sister of the above four patients, and like them of short stature, was admitted to hospital in September, 1952. Three years prior to admission she experienced one episode of renal colic and hematuria; a stone was removed. She had one child, no other pregnancies. A nodule, two cm. in diameter, was palpable in

left lobe of thyroid. Serum calcium 15.8 mg.%, serum phosphorus 2.1 mg.%, alkaline phosphatase 0.4 Bodansky units. No skeletal changes, no renal changes found on radiological scrutiny. As in Case XII, an adenoma attached to the capsule of the left superior lobe of the thyroid gland (1.0 by 0.8 by 0.6 cm. and 1.9 grams) and an other adenoma fused with the right superior thyroid pole (diameter 0.9 cm., weight 86.5 mg.) were located and removed. Latent tetany was elicited on the second post-operative day.

The earlier than average age of clinical manifestation of primary hyperparathyroidism, the similarity of adenoma structure (predominately dark oxyphil cells) in all five patients, the proved multiplicity of adenomas in four cases and the probability of dual tumors in the fifth, the shortness of stature, the absence of other abnormalities such as pituitary tumors, islet cell tumors, or duodenal ulcers are the common denominators in this family. Unlike the previously reported familiar cases with primary hyperparathyroidism, a variation in location of the adenomas from the inferior position is exhibited within the family but only in those cases proven to have possessed two parathyroid adenomas. No studies to exclude environmental factors were performed where calcium had been regularly supplied in the diet, skeletal changes were minimal or nil.

A study by *Moldawer, Nardi, and Raker* describes a father and daughter, each with multiple parathyroid adenomas. The father showed symptoms indicative of a pituitary tumor; from his daughter two pancreatic islet cell tumors have been removed.

CASE XIV (*Moldawer et al.*): 22-year-old female was found comatose in bed, with provisional diagnosis of subdural hematoma she was admitted to hospital. Five years previous she had suffered concussion in an automobile accident. Since then she had been plagued by bouts of nausea, vomiting, and frontal headache. Three days before admittance patient was unconscious, and according to mother "twitching over entire left side of body". Six months ago, she passed a number of small stones in her urine. Appetite had been voracious, but no weight gained. Urinalysis normal except for 8-10 erythrocytes per high dry microscopic field. Three days after admission patient was unresponsive in morning. She had had prolonged period of irrationality previous day. Left pyramidal signs present. Fasting blood sugar value was 29 mg.%, serum calcium 12.8 mg.%, serum phosphorus 2.2 mg.%; marked negative calcium balance. Roentgenogram showed small stone in lower pole of right kidney. All bones were normal. Subtotal pancreatectomy yielded two islet cell adenomas. Several weeks later three enlarged parathyroid glands were found on cervical exploration. The upper and lower left-side glands were completely removed, and a subtotal resection of the slightly enlarged right lower gland was performed. The upper left gland measured 6 mm. in diameter and was 3 mm. thick; the lower left gland 6 by 7 by 4 mm. These were definite adenomas.

The section of the right lower gland was insufficient in size for diagnosis. No complications thereafter.

The expression of the hyperinsulinism antedates the first symptoms of hyperparathyroidism by $4\frac{1}{2}$ years. As has been shown by *Moldawer*, insulin decreases the serum phosphate, probably through increasing glucosephosphate levels raising the serum calcium. Thus one would expect a depression of parathyroid activity.

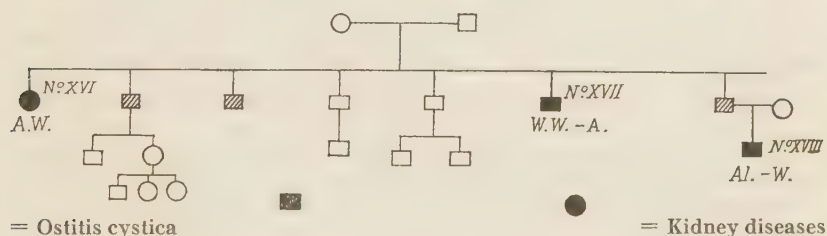
Where adenomas of pancreas and parathyroid occur together, multiplicity can be expected in both glands (*Underdal et al.*).

CASE XV (*Moldawer et al.*): A 36-year-old male, with three-year history of left upper abdominal pain recurring before meals and relieved by food or milk, after a negative gastrointestinal series, underwent a laparotomy. No ulcer found. Three months later after hematemesis a *duodenal ulcer* was diagnosed roentgenologically. Following a second episode of hematemesis, a subtotal gastrectomy and an anterior gastro-jejunostomy were performed. Following a third hemorrhage from a marginal ulcer further gastric resection was carried out with a jejuno-jejunostomy and an anterior gastro-jejunostomy. Further bleeding occurred and transthoracic vagotomy was performed. His mother had had "ulcer trouble" for many years, and one brother had died following hemorrhage from an ulcer at age of 28. Pyrosis occurred often. He experienced nightly cramps in both calves, polyuria and polydipsia. Diminished hearing had been noted for the last four years. Also he complained of loss of libido. Hematemesis recurred thrice, followed by a generalized convulsive seizure. The skin was thin, hair fine and generally reduced, especially on face, axillary and pubic areas. The testes were soft and small. A papilloma was noticed on left ear. Abnormal laboratory reports: erythrocytes 2.9 million, hematocrit 34%. Urine specific gravity could not be raised above 1,005 despite dehydration and pitressin. Serum calcium, drawn because of his daughter's history, was 12.1-13.1 mg.%, serum phosphorus 1.4-3.0 mg.%, alkaline phosphatase 3.0-5.4 Bodansky units/100 c.c. blood. Gastro-intestinal examination showed deviation of the esophagus to the right of the midline in the midcervical region and demonstrated ulceration in jejunum opposite anastomosis. Skeletal demineralisation was present. The sella turcica was enlarged. Neck exploration revealed *parathyroid adenomas* in upper and lower left glands, which were removed. The former measured 0.6 cm. and the latter 1.5 cm. in diameter. The right lower parathyroid gland was not located with certainty. Two years later symptoms of confusion, headache, spells of anxiety, sweating, and weakness occasioned re-admission. There had been threats of suicide. Only medication at that time was antacid therapy. Laboratory studies were normal except for one elevated serum calcium. With the diagnosis reactive *depression* the patient was discharged. During first night at home the patient awakened with great thirst. Nausea and hematemesis followed. Gastrosocopy revealed hemorrhagic gastritis; total *gastrectomy* was performed. Reexploration of the parathyroids was deferred. Patient wished to defer all other studies indefinitely.

Did a third, an aberrant parathyroid adenoma exist? The absence of tetany would substantiate this conclusion, but from the above histories it is clear that tetany manifestation is no absolute criterion for complete removal of hyperfunctioning parathyroid tissue. The anatomical location pattern seen in the daughter, though no surety of the adenomatous nature of the right inferior gland was available, and the partial repetition of the pattern in her father plus the frequency of aberrant location of especially the inferior parathyroid glands (*Norris*), speak for a persistent adenoma. The single high serum calcium could have been explained by the decreased phosphorus absorption following antacid therapy. The similar incidence in three persons of this family will be discussed later.

III. A new example of familial hyperparathyroidism

is presented here. In Basel, Switzerland, there exists a family, in which *three members*, two siblings and their nephew, have been afflicted with *osteitis fibrosa cystica generalisata*, three had *nephrolithiasis*, one *gallstones*, one a *renal anomaly* and one *nephrocirrhosis*.



In the first generation the father succumbed to the complications of a rectal carcinoma, aged 66, the mother, at 73 years, departed subsequent to an apoplectic attack. Though no history of fractures or rachitis is recorded, the mother possessed "O" legs, genu varum. The sclerae of both eyes were of bluish colour, though no symptoms characteristic of osteogenesis imperfecta or otosclerosis were present.

In the *second generation* were among 7 children 2 proven cases of Osteitis fibrosa cystica, 3 had renal diseases, as shown in the following record:

No. 1 sister = case XVI died in the age of 33 years from *osteitis fibrosa cystica* with spontaneous fractures, osteoporosis and anemia.

No. 2 brother, died with 44 years, from *nephrocirrhosis*.

- No. 3 brother, departed with 18 years from lung tuberculosis, showed on autopsy a *kidney anomaly* (= Kuchenniere).
 No. 4 brother, living, 55 years, had *gallstones*.
 No. 5 brother, living, 54 years, no diseases.
 No. 6 twin-brother = case No. XVII, living, 52 years, had *nephrolithiasis* and *Ostitis fibrosa cystica* with operation of a parathyreoidea adenoma with 40 years.
 No. 7 twin-brother of No. 6, living, 52 years, had *nephrolithiasis* with 34 years, at present no troubles. Albuminuria 0.5%, tension 150/105, Calcium 10.8 mg.‰, urea 45 mg.‰, normal pyelogram.

Third generation:

The son of No. 7 had hyperparathyroidism with *nephrolithiasis* 2 years ago. *Parathyroid adenoma* was removed. = Case XVIII.

Two proven cases of *osteitis fibrosa cystica generalisata* are present in this family: the first a severe "Recklinghausen", the second characterized by a dramatic post-operative course:

CASE XVI (published by Moser): 33-year-old female (A. We.), who like her mother possessed blue sclerae, emaciated, with unusual extremity deformities.

No rachitis. First walk at age of one year.

Menarche 12 years. Menses regular until twentieth year, then hypermenorrhea and dysmenorrhea, accompanied with emesis.

Till eighteenth year healthy, then gripe followed by pains while walking and standing, that disappeared after shoe arches were employed.

At age of 26 years, patient fell down stairs; resultant contusion healed without incident. Because of nervous shock patient bedridden six months. During this period weight loss and constant fatigue. Frequent emesis without special cause. Gradually increasing disturbance on walking. Severe pain in heel and knee.

One year after accident distinct swelling of left heel; limping. Vertebral column discomfort. Bending, then standing on left leg impossible.

Soft, then solid swellings on tibia, sternum and wrist joints that were painful to pressure.

In her twenty-ninth year, subsequent to fall on left upper arm, fracture here and spontaneous fractures of right tibia and fibula. Healing protected. Scraping of fractured areas. Histological diagnosis: *osteitis fibrosa cystica generalisata*.

A large tumor apparent at this time on right ilium.

Therapy included blood transfusions, phosphor, Fowler's solution, and extension of the extremities.

Blood examination: hemoglobin 43‰, W.B.C. 11,008, differential count normal. Blood Calcium 15.98 mg.‰.

Urine: macroscopically cloudy. The sediment consisted of calcium salts. No glycosuria, no albuminuria.

Roentgenograms: skull and epistropheus showed rarefactions; ribs: multiple globular cysts; clavícula: demineralization; vertebral column, especially

lumbar region: osteoporosis; innominate bones: rarefaction and large cyst formation; right scapula: large cyst; right humerus head: fracture; middle phalanges: disappearance of radial corticalis; right femur: irregular demineralization with indistinct transition from epiphysis to diaphysis; fracture of right tibia and fibula (spontaneous fracture, vide supra) with callus formations; left fibula and tibia: numerous cysts; left calcaneus: large cyst.

The patient died on January 14, 1931. On the right inferior parathyroid an encapsuled tumor, about the size of a walnut ($3,1 \times 3,0 \times 1,2$ cm.) was located at autopsy. A superior left parathyroid tumor, the size of a filbert ($1.0 \times 1.0 \times 0.4$ cm.), was also found. Histological examination showed both tumors to be parathyroid adenomas of the oxyphilic variety.

Skeletal findings at autopsy: skull: hyperostotic—porotic thickening; vertebral column characterized by thickening and extreme shortening of whole body (120 cm.). Extremities: numerous fractures and thickenings. Bone substance so soft, that it could easily be cut by knife. The right scapula had lost its original form. Histologically the trabecular and lamellar arrangement was irregular. The marrow was composed of elongated and round cells.

Other findings at necropsy: heart: brown atrophy; aorta: no sclerosis or calcium deposits; lung: terminal edema; kidneys: widespread calcium deposits in medulla; cortex: fibrosis of glomeruli and round cell infiltration; renal pelvis contains calcium sands; ovaries atrophic; adrenal cortex: fatty deposition especially in zona fasciculata.

Epicrisis: a severe progressive bone disease ranging over fifteen years, commencing four years after puberty and culminating in death of 33 year old female. (Seldom does hyperparathyroidism appear before puberty). Through clinical, roentgenological, and histological investigation osteitis fibrosa cystica generalisata was diagnosed. Tumors, cysts and rarefactions widely distributed.

Her younger brother presented another case of hyperparathyroidism (XVII), published by *Merke*.

CASE XVII: 40 years old male (W.W.A.). Fifteen years previous to hospital admission phosphate stone was removed operatively from left kidney. Ten years later, because of pyelonephrosis, left nephrectomy.

Frequent ischialgia.

Three years following nephrectomy fracture of the neck of the left femur. Roentgenograms showed demineralization and cysts in femur and innominate bones.

Marked hypercalcemia, 13.5 mg.%. Consolidation of fracture protracted. First cast, then cane necessary for walking.

In last few months before admittance slight discomfort in left forearm and increasingly intense pain in lower leg. The gait, wobbly; walking possible only with some support such as a walking stick. Fatigue. No desire to work.

Admission to St. Clara Hospital, Basel (Prof. *F. Merke*). Following status then recorded:

Normal stature. Well nourished middle-aged male.

Neck: bilateral nodular goitre.

Thorax: slight kyphosis and scoliosis of thoracic vertebrae.

Abdomen: left nephrectomy scar; no reaction at site of scar.

Extremities: left leg shortened 2 cm. Slight flexion hindrance in left hip and knee joints. No atrophy of musculature. No circumscribed tumors palpable, though left tibia in its middle third appeared diffusely thickened and was painful to touch.

Blood: no essential morphological changes. Sedimentation rate 4/18 mm. in first and second hour. Blood calcium 13.4 mg.%, phosphor 1.8 mg.%, alkaline phosphatase 68 Bodansky units (suggesting active osseous alterations).

Urine: specific weight 1.014. Trace of albuminuria. Sugar negative. Slight sediment, epithelial cells and leucocytes. Calcium excreted in urine 3.6-5.6 g. pro die. Phosphorus excreted in urine daily 2.6-3.6 g.

Roentgenograms: left femur neck showed pseudoarthrosis with elevated trochanter. In innominate and upper left femur large distinct cysts. Left humerus: demineralization; ulna, radius, and carpal bones possessed diffuse demineralization with partially "moth-eaten" corticalis.

At operation a bilateral nodular colloid struma present. On dorsal side of the right inferior pole of the struma a *cystic parathyroid tumor*, the size of a cherry, 2.2 by 2.4 by 1.0 cm., containing dark brown fluid, was removed, and a portion of the right thyroid resected. On the dorsum of the left lower lobe of the thyroid a *second extracapsular parathyroid tumor*, twice the size of the other, was *also removed* (5.0 by 4.0 by 2.1 cm.) along with portion of left struma.

Histological examination proved that both parathyroid adenomas were composed predominately of wasserhelle cells of varying size.

Third postoperative day: oliguria (150 cm.) with NPN 96 mg.%. With parathormone injections diuresis commenced and during the sixth day reached 1,500 cm. NPN 43 mg.%.

Eight postoperative day: tetany (*Chvostek*, *Trousseau*), hyperactive reflexes, muscular twitching and spasms, risus sardonius. AT 10 and calcium injections increased the blood calcium levels though hypocalcemia remained throughout next three months.

Psychosis due to tetany appeared on twelfth postoperative day: unrest, depression and paranoid delusions alternating with euphoric phases; urinary and fecal incontinence. The psychosis and tetany phenomena terminated on twentieth day.

On the same day spontaneous fracture of right femur. Consolidation slow. A tibial biopsy four months after operation was so soft that it could easily be cut by a knife. Histologically the section was typical of osteitis fibrosa, with demineralized fibrous trabeculae and numerous wide osteoclastic borders.

After six months, roentgenogram showed beginning remineralization of bones.

Epicrisis: At 25 years of age W. W.-A. has a phosphate stone removed operatively from left kidney. Ten years later following

pyelonephrosis, nephrectomy. Two years prior to parathyroidectomy, fracture of femur neck, at which time roentgenograms reveal skeletal changes in form of multiple cysts. The fracture heals as a pseudo-arthritis. Hypercalcemia; increasing osseous pain, especially in right calf. On hospital admission the nature of the disease first recognized. After removal of both parathyroid adenomas oliguria, tetany, and psychosis appear. Slow rise to normocalcemia. Healing.

The nephrolithiasis fifteen years previous to the parathyroidectomy was most probably a manifestation of latent hyperparathyroidism. Though pathological examination revealed some parathyroid hyperplasia (frequent in most parathyroid adenomas), the oxyphilic adenomas dominated the histological picture. There is evidence in at least *one other member* of this family of a kidney anomaly, an ectopic, flattened kidney with hilus rotated laterally and upward (*Kuchenniere*). This brother died of pulmonary tuberculosis. There was no evidence of hyperparathyroidism. *Another brother*, a dizygotic twin of our patient A. W.-A., suffered from *pyelonephrosis*. During the last decade constant albuminuria, otherwise no symptomology. Pyelograms were normal. Here again no evidence of "Morbus Recklinghausen".

The skeletal changes of W.W.-A. developed two years previous to operation. This accelerated course may be attributed to a rapidly progressive growth of both tumors, though the lack of degenerative changes in the adenomas speaks for a more gradual growth. Either by increased phosphate or increased calcium intake (one liter of milk yields 1 gram calcium approximately) bone demineralization could have been prevented. However, neither high phosphate nor high calcium consumption is advisable therapy in cases of osteitis fibrosa generalisata. Both may lead to metastatic calcification (hyper-hyperparathyroidism or parathyroid poisoning) and renal calculi.

The tetany after parathyroidectomy usually follows within 24 to 48 hours. It may last days or years. It appeared in W. W.-A. on the eighth postoperative day; the delay due to the oliguria. *Merke* believes that where two parathyroid adenomas are found and where renal function has been shown to be impaired or only one kidney is present, the second adenoma should be removed at a later operation.

CASE XVIII: Al. W., born 1933, male, 25 years old (son of No. XVII), no siblings, nephew.

Personal history: at 14 years of age luxated double forearm fracture. Three weeks later operative reposition. Sixteenth year gastritis, polydipsia, no glycosuria.

During twenty-second year angina followed by renal colic. Pyelitis. Two *phosphate calculi* removed per vias naturales, but continual pain persists in kidney area.

Seven months later again angina and colic. Pyelogram and cystoscopy normal. Bleeding on micturition lasting three weeks. Urine cloudy.

Frequent pyalism, dyhidrosis (hands), and polydipsia during last seven years.

Patient drinks up to two liters milk pro die.

Patient referred to the Basel University Policlinic where *hyperparathyroidism* was diagnosed. When seen in the Policlinic the following status was recorded:

Stature: slightly below normal; general condition: good; the patient appears to be somewhat labile in temperament.

Neck: no struma, no glands.

Heart: Tachycardia, accentuated second tone, very soft first tone. EKG shows shortened ST. Blood pressure 160/120. Puls 110/min., regular.

Abdomen: pain on pressure in left kidney region.

Extremities: reflexes very active. No tumors, no pain.

Urine: cloudy. Sediment consists of a few epithelial cells and cristals of calcium phosphate. Urobilinogen positive.

Kidney function test: good dilution, after one liter tea specific weight reduced from 1,010 to 1,000.

Phenol red test normal: first hour 55% of dye excreted (normal 40-70%); second hour 7.1% (5-10%).

Creatinine clearance test: 94.6 c.c. (80-90 c.c. normal).

Sulkowitch + + + +.

Blood examinations: serum calcium 15.3 mg.%, serum phosphorus 1.6 mg.%, alkaline phosphatase 5.1 Bodansky units. Blood creatinine 1.31 mg.%. Alkali reserve 60.5%.

No skeletal demineralization or cyst formation seen on roentgenograms. No calculi shadows in renal area. Calcium shadow paravertebrally near right innominate bone.

On March 21, 1956, Professor *F. Merke* removed a *parathyroid adenoma*, the size of a cherry, from the right lower pole of the thyroid gland, which was normal. The tumor was not connected to the thyroid. A prominent grey nodule protruded from the lower left portion of the thyroid. Though most likely this was thyroid tissue, a small section was removed for histological examination.

Pathological report: 2.5 by 2.0 by 1.5 cm., cystic tumor with mucous contents. The adenoma was composed predominantly of wasserhelle cells, some of which possessed eosinophilic protoplasm. The section from the lower left thyroid pole was typical thyroid tissue, microfollicular with eosinophilic colloid contents.

Second postoperative day: Carpopedal spasms. Chvostek negative. Calcium and parathormone administered. The attack of tetany was repeated the next day. Calcium i.v. The following day AT 10 administered. On sixth postoperative day again parasthesia in hands. There were no further developments, and patient was released from hospital April 7, 1956.

One month later serum calcium 9.4 mg.%, serum phosphorus 2.0 mg.%, alkaline phosphatase 3.6 units.

At this time (July, 1958), patient occasionally experiences paresthesia in the hands; also occasional lower right abdominal pains. The serum calcium 10.0 mg.% and phosphorus and the serum protein values are normal. Vasoneurotic cephalalgia.

Epicrisis: Intermittent history of renal colic over twelve months' period in young male patient (22 years) before hyperparathyroidism diagnosed. His aunt and uncle both had been previously diagnosed as cases of osteitis fibrosa cystica generalisata. Right inferior wasserhelle cell adenoma of parathyroid removed.

IV. Discussion.

How do the adenomas occurring in familial hyperparathyroidism compare with parathyroid adenomas generally in respect to location, multiplicity, histological structure, age and sex distribution? Table I resumes the essential facts of all 17 known familial cases.

The *location* of adenomas in familial hyperparathyroidism is available in the literature: 8 superior, 15 inferior and 1 substernal. *Castleman* and *Mallory* found approximately 15% of all the parathyroid adenomas to be in the superior position. The most frequent sites in familial cases are the left inferior position (9 adenomas), left superior and right inferior (6 each). Generally non-familial adenomas are found most frequently in the same positions. Abnormal position of the tumors of the parathyroid are reported in 25% of all cases. In the family statistics regarding the adenomas only one substernal neoplasm was found fifteen years after removal of a primary left inferior adenoma. The chance of superimplantation, although remote, is nonetheless present. The fact that less often ectopic parathyroid adenomas exist in familial hyperparathyroidism enhances the view that at least one systemic factor is present in hereditary hyperparathyroidism; the ectopy is indicative of embryonal rest cells that under lack of growth restraint and in response to various stimuli develop into neoplasms.

TABLE I.

Geographical location	Age and sex	Relatives also effected.	Serum Calcium mg %	Location of tumor	Size	Path.	Miscellaneous
I 30 California	17 years ♀	brother (II)	19.20	left lower	3.0 × 3.7 × 2.8 cm. 11.8 g.	wasserhelle adenoma	
II 30 California	23 years ♂	sister (I)	17.5	left lower	3.0 × 2.0 × 2.0 6.5 g.	chief cell adenoma	
III 31 Ohio	20 years ♀	sec. cousin (IV)	---	---	3.5 g.	dark oxyphile adenoma	
IV 31 Ohio	? ♀	sec. cousin (III)	---	---	---	dark oxyphile adenoma	
V 28 Norway	47 years ♀ 15 years symptoms	sister (VI)	14.0	left lower	4.0 × 2.5 × 2.5 cm.	dark oxyphile adenoma	
VI 28 Norway	33 years ♀	sister (V)	14.0	no tumor found			patient died 7 years later of uremia
VII 32 Pennsylv- ania a)	35 years ♂	daughter (VIII)	13.0	left lower	3.3 × 3.1 × 3.2 cm.	wasserhelle adenoma	12 years prev. duodenal ulcer
b)	50 years ♂		15.8	substernal	4.2 × 2.6 × 2.3 cm.	wasserhelle oxyphile chief cell	adenoma
VIII 32 Pennsylv- vania	13 years ♀	father (VII)	13.4	left lower	2.7 × 2.5 × 2.2	chief cell adenoma	died probably of cerebral hemorrh.

IX 33	Montana	25 years ♀	15.68	right lower	$3.0 \times 2.0 \times 1.3$	dark oxyphilic adenoma	5 years after para-thyroidectomy renalcolic and signs of renal insufficiency
X 33	Montana	25 years ♀	14.4-19.5	right lower left upper	$3.5 \times 2.0 \times 2.0$ (12 g.) $1.5 \times 1.0 \times 1.0$ (1.2 g.)	dark oxyphile	2nd operation 7 months after first staghorn calculus left nephrectomy previous to para-throidectomy
XI 33	Montana	29 years ♂	13.3-13.6	left lower right lower	$1.9 \times 1.3 \times 1.2$ (1.5 g.) $1.3 \times 0.9 \times 0.8$ (0.6 g.)	dark oxyphile	
XII 33	Montana	30 years ♀	16.8-18.1	right upper left upper	$1.5 \times 1.0 \times 1.0$ (2.5 g.) $2.5 \times 2.0 \times 1.7$ (6.0 g.)	dark oxyphile	
XIII 33	Montana	26 years ♀	15.8	right superior left superior	0.9 cm. diam. (80 mg.) $1.0 \times 0.8 \times 0.6$ cm. (1.9 g.)	dark oxyphile	
XIV 34	Massachusetts	22 years ♀	12.8	left upper left lower right lower?	$3.0 \times 6.0 \times 6.0$ mm. $6.0 \times 7.0 \times 4.0$ mm.	? ? ?	multiple islet cell adenomas of pancreas removed
XV 34	Massachusetts	36 years ♂	12.1-13.7	left upper right lower not located	0.6 mm. diameter 1.5 mm. diameter	? ? ?	enlarged sella turcica, some symptoms of pit. tumor, repeated peptic ulcers

TABLE I (continued).

	Geographical location	Age and sex	Relatives effected	Serum			Tumor			Miscellaneous
				Ca mg %	P mg %	Alk. Phosphate Bodansky	Location	Size cm	Histological Structure	
XVI A. W.	Basel, Switzerland	33 years ♀	brother (XVII) nephew (XVIII)	15.98	—	—	right lower left upper	$3.1 \times 3.0 \times 1.2$ $1.0 \times 1.0 \times 0.4$	{ oxyphile adenoma	Severe osseous deformity leading to exitus
XVII W. W.-A	Basel, Switzerland	40 years ♂	sister (XVI) nephew (XVIII)	13.4	1.8	68	right lower left upper	$2.2 \times 2.4 \times 1.0$ $5.0 \times 4.0 \times 2.1$	{ wasserhelle adenoma	kidney stones, nephrectomy, coxal pseudoarthrosis, post-operative spontaneous fracture, post-operative tetany and psychosis
XVIII AL. W.	Basel, Switzerland	25 years ♂	aunt (XVI) uncle (XVII)	15.3	1.6	5.1	right lower	$2.5 \times 2.0 \times 1.5$	wasserhelle adenoma	prolonged healing of arm fractures at 14 years. Gastritis at 16 years. Post-operative tetany

That over 50% of the cases of hereditary hyperparathyroidism present *two or more adenomas* in comparison with the 8-10% of cases of all hyperparathyroid patients lends more credence to the assumption that a systemic factor is responsible in the former.

Within five of the seven families there is variance in the location of the adenomas. When two or more adenomas occur in a family member, it is not obligate for the other member (or members) afflicted with hyperparathyroidism to possess the tumor (or tumors) at exactly the same site.

Histological difference in the adenomas can be seen in 6 of the 7 families. Perhaps these intracellular morphological differences are expressions of various states of endocrine activity, the wasserhelle cells being in intermediate position between the chief cells (greatest secretion of parathormone) and the oxyphilic cells. The 22 adenomas in the accompanying table showed 14 oxyphile, 5 wasserhelle, 2 chief cell, and one mixed adenoma. Where two adenomas were removed simultaneously from one patient, their histological structure coincided. Generally considering all cases of hyperparathyroidism, the chief cell type of adenoma is most frequently encountered, though the other types and combinations of all types have been found. The size of the various adenomas in the same family showed variance, also the serum calcium values. Clearly extrinsic factors combined with a general systemic factor are responsible for the manifestation of hereditary hyperparathyroidism.

With regard to the *higher distribution* of hyperparathyroidism in the female sex, the statistics in all cases of hyperparathyroidism and those of a hereditary nature are approximately the same; two thirds of those afflicted are female. The hyperfunction during pregnancy and the loss of calcium through menstrual bleeding may be responsible. Before puberty the disease seldom exists.

The *clinical manifestations* of hyperparathyroidism occurred in the hereditary cases usually in the *third and fourth decades*. Previous literature dealing with parathyroid adenomas in general gives 30-60 years of age as the period of greatest frequency. Females are usually affected in the fifth, males in the fourth decade. That the adenomas were found in an age group not completely representative of the largest incidence of expression of this entity is support for a systemic factor, albeit it does not wholly exclude

exogenous factors. Commencement of expression of the disease in the same family has varied also, underlining the importance of external circumstance.

Geographical distribution of familial hyperparathyroidism is varied: Norway, north-east United States (2 families), farwestern U.S. (Montana), California, and Switzerland (Basel). With the exception of Montana these are all heavily industrialized areas. The lack of sunlight, and subsequent low vitamin A levels may well play an accessory role. The three patients in Basel were all employed indoors.

The *incidence of peptic ulcer* in patient XII and in his mother and brother may be more than coincidental. In case VII there is also history of duodenal ulcer. Both these patients were male, in both gastro-intestinal symptoms anteceded other more common complications of hyperparathyroidism, and both patients had multiple (or at least two) parathyroid adenomas. The literature from 1925 onward gives little specific information concerning the occurrence of crises gastriques in the immediate families of patients with primary hyperparathyroidism. Cases reported by *Morelle* and *Beyerink* were characterized by gastro-intestinal symptoms, high serum calcium and minimal or normal skeletal and renal states. Where multiple endocrine adenomas of the pituitary, pancreas, and parathyroid have occurred simultaneously in 6 cases of *Underdahl*, *Woolner*, and *Black*, four of the cases had specific mention of family history. One patient with hyperparathyroidism and hyperinsulinism had a sister who died in coma after experiencing spells of unconsciousness. A second patient, with roentgenologic evidence of intrasellar tumor, hyperparathyroidism, duodenal ulcer, and suspected hyperinsulinism, had a father and a sister with peptic ulcer. A third patient with hyperparathyroidism, peptic ulcer, hypoglycemia, and metastatic bronchial adenoma, had one brother with renal stones and carcinoma of the tail of the pancreas and a father who had had a peptic ulcer. The fourth of these patients had a chromophobe adenoma, three parathyroid adenomas, multiple islets cell adenomas, and a peptic ulcer. This patient had three uncles who had died of brain tumor, a sister with suspected tumor of the pancreas, and a father with duodenal ulcer. *Wermer* reports a father with pancreatic tumors and peptic ulcer. Two of his four daughters had suggestive evidence and a third had necroptic proof of parathyroid adenoma; the three daughters each had peptic ulcer.

The *coexistence of peptic ulcer* in these patients or their relatives points to a hereditary factor causing anomalous development in the embryonic digestive tube. *Coupling of parathyroid adenomas and peptic ulcer with pancreatic cell adenomas and pituitary adenomas* enhances this opinion. The differentiation of the parathyroid, pancreatic islets, and anterior pituitary (*Wermer*) occurs at approximately the same period. It is possible that one gene is responsible for the complex, or variations thereof depending on environmental conditions present. Since both males and females are affected the gene is probably autosomal. In no cases were both parents consanguinous; it is unlikely that such a rare gene would occur in both. The symptoms can be traced through at least two generations, and often several siblings were affected. The gene is then dominant, and it possesses a high degree of penetrance and expressivity. There is a case on record where from a seemingly normal lineage achondroplasty (*Stephans*) occurred. This was explained by a mutation that finds phenotypic expression in the next generation. This may have happened here.

Credence to the hereditary aspect of some cases of parathyroid adenoma will be given by the first recorded case of hyperparathyroidism occurring in twins. The familial incidence of these adenomas, demonstrated in 7 families, plays just now in favour of a hereditary genesis of the idiopathic hyperparathyroidism. Whereas in the remarkable Montana family 5 out of 7 siblings were affected, in Basel 2 of 7 children were hyperparathyroid patients. This difference in penetrance of one or more autosomal genes in these families has yet to be explained. Various environmental stimuli afford the most convenient answer.

Summary.

Primary familial hyperparathyroidism has been previously described six times. The details of these publications are given. In the seventh family which is reported here 2 of 7 siblings and their nephew had hyperparathyroidism. 5 of the other siblings had renal diseases. The possibility of a systemic factor predisposing to parathyroid adenoma formation, but modified by external factors, is discussed.

Zuerst wird in einer detaillierten Darlegung auf die bisher bekannt gewordenen 15 Fälle in 6 Familien mit familiärem Vorkommen von Hyperparathyreoidismus hingewiesen und speziell auf die Kombination der Parathyroideaadenome mit Adenomen der Pankreasinseln und der Hypophyse sowie Magen/Duodenalulcera aufmerksam gemacht. Dann wird über eine 7. Familie, die in Basel zur Beobachtung kam, berichtet. Es fanden sich Ostitis fibrosa cystica generalisata bei zwei Geschwistern und deren Neffen und unter den 7 Geschwistern fünfmal Nierenleiden. Es handelt sich um folgende 7 Geschwister:

1. Eine mit 33 Jahren an Ostitis fibrosa cystica generalisata gestorbene Schwester mit multiplen Spontanfrakturen und schweren Skelettdeformationen. Das Leiden begann mit 18 Jahren, zeigte langsam progredienten Verlauf. Bei der Autopsie fanden sich zwei Parathyroideaadenome von Walnuß- bzw. Bohnengröße und von eosinophilem Typ sowie Kalkinfarkte in beiden Nieren.

2. Ein Bruder starb 44jährig an Nephrosklerose.

3. Ein Bruder, der mit 18 Jahren an einer Lungentuberkulose gestorben ist, wies eine Kuchenniere auf.

4. Ein Bruder lebt mit 55 Jahren und leidet an Gallensteinen.

5. Ein 54jähriger Bruder ist gesund.

6. Ein Zwillingbruder, jetzt 52jährig, litt mit 25 Jahren an Nephrolithiasis, hatte damals operative Entfernung eines Phosphatsteins aus dem linken Nierenbecken, mit 35 Jahren Nephrektomie wegen Pyelonephrose, mit 38 Jahren pathologische Schenkelhalsfraktur mit Cysten und mit 40 Jahren operative Entfernung von 2 Parathyroideaadenomen, histologisch mit wasserhellen Zellen (publiziert von *Merke*), seither beschwerdefrei.

7. Der andere Zwillingbruder hatte mit 34 Jahren eine Nephrolithiasis, zeigt jetzt mit 52 Jahren eine Nephrosklerose mit beträchtlicher Hypertonie ohne Störungen im Kalkstoffwechsel.

Dessen Sohn, Fall 18, also der Neffe der Fälle 16 und 17, mit familiärem Hyperparathyreoidismus, hatte mit 22 Jahren intermittierende Nierenkoliken und Abgang von Phosphatsteinen per vias naturales. Es wurde ein Hyperparathyreoidismus diagnostiziert mit Serumcalcium 15,3 mg%, Serumphosphor 1,6 mg%, stark positivem Sulkovitch-Test im Urin, ohne Cysten im Skelett. Die Stoffwechselstörung ist seit der operativen Entfernung eines Parathyroideaadenoms mit 23 Jahren jetzt bald 3 Jahre behoben.

Anschließend werden die Adenome beim familiären Hyperparathyreoidismus den sonst vorkommenden Parathyreoideaadenomen vergleichend gegenübergestellt in bezug auf Lokalisation, Multiplizität, Histologie, Alter, Geschlecht usw. Bei den familiären Adenomen sind die multiplen Parathyreoideaadenome ca. 5mal häufiger. Zu den hereditären Formen sind exogene Einflüsse anzunehmen, die zur Manifestation des Leidens führen.

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